

APPENDIX A

PCT/US2004/030921 Article 19 Amendment

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Atty Docket No.: 2003946-0221 Client Ref.: HEAT-CIP/US NATL



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Applicant:

Eisai Co., Ltd.

Intl. Appln. No.:

PCT/US2004/030921 Claiming priority to: USSN 10/667,864, filed 22 September 2003

Intl. Filing Date:

22 September 2004

Title:

HEMIASTERLIN DERIVATIVES AND USES

THEREOF

Please see the attached Letter for PCT Article 19 Amendment of Claims, Statement under Article 19(1), Substitute Sheets, and Appendix A-Marked up copy of claim replacements.

Please acknowledge receipt of these documents.

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ATTORNEY'S DOCKET NO.: 2003946-0168 (HEAT/PCT2) IN THE INTERNATIONAL BUREAU (WIPO)

Applicant:

Eisai Co., Ltd.

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Intl. Filing Date:

22 September 2004

Title:

HEMIASTERLIN DERIVATIVES AND USES THEREOF

VIA FACSIMILE (#011-41-22-740-14-35) **CONFIRMATION BY** INTERNATIONAL COURIER

International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20 **SWITZERLAND**

TRANSMITTAL TO THE INTERNATIONAL BUREAU (WIPO)

Please find enclosed the following documents in the above-referenced application:

- 1. Letter for PCT Article 19 Amendment of Claims (PCT Section 205) (2 pages);
- 2. Statement under Article 19(1) (1 page);
- 3. Substitute Sheets (10 pages, including cover page); and
- 4. Appendix A Marked-up copy of claim replacements (10 pages, including cover page).

Date: 13 September 2005

Nadège M. Lagneau, Ph.D.

Attorney Docket No.: 2003946-0168 Client Reference No.: HEAT/PCT2

Agent for Applicant Reg. No.: 51,908

PATENT DEPARTMENT CHOATE, HALL & STEWART LLP Two International Place Boston, MA 02110

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ATTORNEY'S DOCKET NO.: 2003946-0168 (HEAT/PCT2) IN THE INTERNATIONAL BUREAU (MIRO) 1 10 21 MAR 2006

Applicant:

Eisai Co., Ltd.

Intl. Appln. No.:

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Intl. Filing Date:

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Title:

HEMIASTERLIN DERIVATIVES AND USES THEREOF

VIA FACSIMILE (#011-41-22-740-14-35) **CONFIRMATION BY** INTERNATIONAL COURIER

International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20 **SWITZERLAND**

LETTER FOR PCT ARTICLE 19 AMENDMENT OF CLAIMS (PCT SECTION 205)

- Applicant herewith submits substitute sheets number 298-300 and 300a-300f to 1. replace sheets number 298-300, originally filed for this application. These substitute sheets are submitted within 2 months of the Notification of Transmittal of International Search Report mailed 13 July 2005.
- Please delete sheets 284-297, as originally filed for this application, and cancel claims 2. 1-45.
- In respect of each claim appearing in the international application based on the 3. substitute sheets submitted herewith, and in accordance with PCT Section 205(b), the following claim(s) is/are:

(i)

Unchanged: Claim 53 is unchanged;

(ii) Replaced:

Claim 46 is replaced with amended claim 46;

Canceled: (iii)

Claims 45, 47-52 and 54-61 are canceled;

(iv) New: Claims 62-81 are new.

A Marked-up Copy of Claim Replacements highlighting the changes is provided herewith as attached Appendix A. Deletions are represented in square brackets, and additions are represented in underlining. Newly added claims are labeled "New".

100072871

Respectfully subflitted,

67770 21 MAR 2006

Date: 13 September 2005

Nadège M. Lagneau, Ph.D.

Agent for Applicant Reg. No.: 51,908

PATENT DEPARTMENT CHOATE, HALL & STEWART LLP Two International Place Boston, MA 02110 Tel: (617) 248-5150

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Applicant:

Eisai Co., Ltd.

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HEMIASTERLIN DERIVATIVES AND USES THEREOF

VIA FACSIMILE (#011-41-22-740-14-35) **CONFIRMATION BY** INTERNATIONAL COURIER

International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20 **SWITZERLAND**

STATEMENT UNDER ARTICLE 19(1)

Applicant respectfully submits that no new matter is presented with the amendment set forth in the "Letter for PCT Article 19 Amendment of Claims" filed concurrently herewith. Specifically, support for claims 62-65 can be found inter alia in Scheme 14 page 105 of the specification as originally filed. Claims 66-68 find support, for example, in paragraph [0124] page 107 of the specification. Claims 69-70 find support, for example, in paragraph [0122] page 106 of the specification. Support for claims 71-77 can be found, for example, in sections d)-j) on page 28 and sections d) and e) on page 29 of the specification. Finally, new claims 62-81 find support inter alia in paragraphs [0106]-[0114] on pages 100-104 of the specification as filed.

Applicant respectfully requests entry and consideration of this amendment in processing the application.

Date: 13 September 2005

Nadège M. Lagneau, Ph.D.

Agent for Applicant Reg. No.: 51,908

PATENT DEPARTMENT CHOATE, HALL & STEWART LLP Two International Place Boston, MA 02110

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- APPENDIX A
Marked-up Copy of Claim Replacements

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Claims 1-45 (Canceled)

46. (Currently Amended) An intermediate for the preparation of a compound having the structure:

wherein g is 1, 2, 3 or 4;

R₂ is hydrogen, or a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl, heteroalkyl, -alkyl(aryl) or acyl moiety;

R₆ is substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

R_{10a} is hydrogen or substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

L is $CR_{L1}R_{L2}$, S, O or NR_{L3} , wherein each occurrence of R_{L1} , R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R_{G1} , R_{M1} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent R_{L1} , R_{L2} , R_{L3} , R_{G1} , R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety; and

wherein said intermediate has the following structure:

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53. (Original) The intermediate of claim 46 having the structure:

Claims 54-61 (Canceled)

62. (New) An intermediate having the structure:

$$\mathsf{R}_{\mathsf{G1}} \overset{\mathsf{R}_2}{\underset{\mathsf{0}}{\bigvee}} \overset{\mathsf{0}}{\underset{\mathsf{N}}{\bigvee}} \overset{\mathsf{R}_6}{\underset{\mathsf{N}}{\bigvee}} \overset{\mathsf{Me}}{\underset{\mathsf{N}}{\bigvee}} \overset{\mathsf{R}^{\mathsf{x}1}}{\underset{\mathsf{R}^{\mathsf{x}2}}{\bigvee}}$$

wherein R^{x1} and R^{x2} are independently hydrogen, aliphatic, alicyclic or aryl; g is 1, 2, 3 or 4;

L is $CR_{L1}R_{L2}$, S, O or NR_{L3} , wherein each occurrence of R_{L1} , R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R_{G1} , R_{M1} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent R_{L1} , R_{L2} , R_{L3} , R_{G1} , R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety;

 R_2 is hydrogen, -(C=O) R_C or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein each occurrence of R_C is independently hydrogen, OH, OR_D , or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein R_D is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

 R_6 is hydrogen, -(C=O) R_E or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, wherein each occurrence of R_E is independently hydrogen, OH, OR_F, or an aliphatic, alicyclic, heteroaliphatic,

heteroalicyclic, aryl or heteroaryl moiety; wherein R_F is an aliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety.

63. (New) The intermediate of claim 62 having the structure:

- 64. (New) The intermediate of claim 62 or 63 wherein R^{x1} and R^{x2} are independently hydrogen, alkyl or aryl.
- 65. (New) The intermediate of claim 62 or 63 wherein R^{x1} and R^{x2} are each hydrogen.
- 66. (New) The intermediate of any one of claims 46, 53, 62 and 63 wherein R_2 is hydrogen, or a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl, heteroalkyl, -alkyl(aryl) or acyl moiety.
- 67. (New) The intermediate of claim 66 wherein R_2 is methyl, ethyl, propyl, butyl, pentyl, tert-butyl, i-propyl, $-CH(CH_3)Et$, $-CH(CH_3)CH_2CH_2CH_3$, $-CH(CH_3)CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH(CH_3)CH(CH_3)_2$, $-C(CH_3)_2Et$, $-CH(CH_3)$ cyclobutyl, $-CH(Et)_2$, $-C(CH_3)_2C\equiv CH$, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl.
- 68. (New) The intermediate of claim 66 wherein R₂ is methyl, ethyl, propyl or i-propyl.
- (New) The intermediate of any one of claims 46, 53, 62 and 63 wherein R₆ is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl, -CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl; and R₂ is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl, -CH(CH₃)Et, -CH(CH₃)CH₂CH₂CH₂CH₃, -CH₂CH(CH₃)₂, -CH(CH₃)CH(CH₃)₂, -C(CH₃)₂Et, -

CH(CH₃)cyclobutyl, -CH(Et)₂, -C(CH₃)₂C≡CH, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl.

- (New) The intermediate of claim 69 wherein R₆ is tert-butyl. 70.
- (New) The intermediate of any one of claims 46, 53, 62 and 63 wherein R_{G1} is 71. hydrogen, substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl or substituted or unsubstituted phenyl.
- (New) The intermediate of claim 71 wherein R_{G1} is hydrogen, methyl or phenyl. 72.
- 73. (New) The intermediate of claim 71 wherein R_{G1} is hydrogen.
- (New) The intermediate of any one of claims 46, 53, 62 and 63 wherein R_{MI} 74. and R_{M2} are each independently hydrogen, hydroxyl, a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl moiety; a substituted or unsubstituted phenyl moiety, or R_{M2} is absent when R_{M1} and the substitutents on L, taken together, form a substituted or unsubstituted aryl or heteroaryl moiety.
- 75. (New) The intermediate of claim 74 wherein R_{M1} and R_{M2} are each hydrogen.
- (New) The intermediate of any one of claims 46, 53, 62 and 63 wherein L is 76. CR_{L1}R_{L2} wherein R_{L1} and R_{L2} are each independently hydrogen, substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl or substituted or unsubstituted phenyl.
- 77. (New) The intermediate of claim 76 wherein L is CH₂.
- (New) A method for preparing a compound of formula VI^A: 78.

said method comprising steps of:

(a) reacting two compounds having the structures:

$$R_{1}$$
 R_{2} R_{1} R_{1}

under suitable conditions to form a compound having the structure:

(b) oxidizing the compound formed in step (a) under suitable conditions to form a compound having the structure:

(c) subjecting the compound formed in step (b) to suitable olefin-forming conditions to form a compound having the structure:

$$R_{G1} + \begin{pmatrix} R_2 & O & R_6 & Me & H & O \\ N & N & N & R_{10a} & R_$$

(d) subjecting the compound formed in step (c) to suitable diversification reactions to generate the desired compound having the structure:

wherein g is 1 or 2;

RQ is hydrogen, lower alkyl or an oxygen protecting group;

R₂ and R₆ are independently substituted or unsubstituted linear or branched lower alkyl;

R_{10a} is hydrogen or substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

L is $CR_{L1}R_{L2}$, S, O or NR_{L3} , wherein each occurrence of R_{L1} , R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R_{G1} , R_{M1} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent R_{L1} , R_{L2} , R_{L3} , R_{G1} , R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

- 79. (New) The method of claim 78 wherein, in the step of oxidizing, the conditions comprise Swern or Dess Martin oxidizing conditions.
- 80. (New) The method of claim 78 wherein, in step (c), the olefin-forming conditions comprise $Ph_3P=C(R_{10a})CO_2R^{Q'}$; wherein $R^{Q'}$ is hydrogen, lower alkyl or an oxygen protecting group; and R_{10a} is as defined generally above and in classes and subclasses herein.
- 81. (New) A method for preparing a compound of formula VI^A:

said method comprising steps of:

(a) reacting two compounds having the structures:

$$R_{2}$$
 R_{3} R_{6} R_{2} R_{6} R_{6

under suitable conditions to form a compound having the structure:

wherein R^{X1} and R^{X2} are independently hydrogen, alkyl, heteroalkyl, aryl or heteroaryl;

(b) converting the compound formed in step (a) under suitable conditions to form a compound having the structure:

$$R_{G1} + V_0 + V$$

(c) subjecting the compound formed in step (b) to suitable diversification reactions to generate the desired compound having the structure:

wherein g is 1 or 2;

RQ' is hydrogen, lower alkyl or an oxygen protecting group;

R₂ and R₆ are independently substituted or unsubstituted linear or branched lower alkyl;

R_{10a} is hydrogen or substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

L is CR_{L1}R_{L2}, S, O or NR_{L3}, wherein each occurrence of R_{L1}, R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R_{GI} , R_{MI} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent R_{L1} , R_{L2} , R_{L3} , R_{G1} , R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

- 79. (New) The method of claim 81 wherein the step of converting comprises steps of:
 - (i) subjecting the compound having the structure:

to ozonolysis conditions to form an aldehyde having the structure:

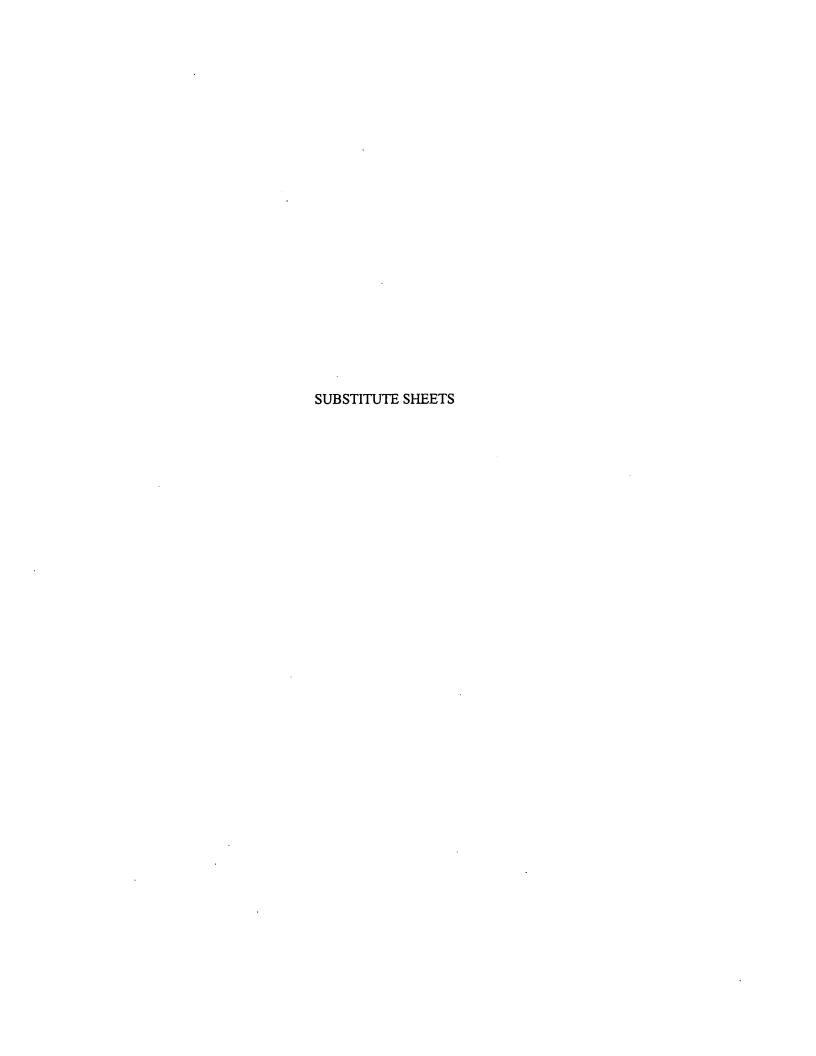
$$R_{G1}$$
 R_{M1} R_{M2} R_{M2} R_{M1} R_{M2} R_{M3} R_{M4} R_{M4} R_{M4}

(ii) subjecting the compound formed in step (i) to suitable olefin-forming conditions to form a compound having the structure:

- 80. (New) The method of claim 81 wherein, in step (ii), the olefin-forming conditions comprise $Ph_3P=C(R_{10a})CO_2R^{Q'}$; wherein $R^{Q'}$ is hydrogen, lower alkyl or an oxygen protecting group; and R_{10a} is as defined generally above and in classes and subclasses herein.
- 81. (New) The method of claim 81 wherein, the step of converting comprises a step of:

subjecting the compound having the structure:

to cross-olefin-metathesis conditions in the presence of $CH_2=C(R_{10a})CO_2R^{Q'}$ to form a compound having the structure:



46. An intermediate having the structure:

wherein g is 1, 2, 3 or 4;

R₂ is hydrogen, or a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl, heteroalkyl, -alkyl(aryl) or acyl moiety;

R₆ is substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

L is $CR_{L1}R_{L2}$, S, O or NR_{L3} , wherein each occurrence of R_{L1} , R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R_{G1} , R_{M1} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and wherein any two adjacent R_{L1} , R_{L2} , R_{L3} , R_{G1} , R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

53. The intermediate of claim 46 having the structure:

62. An intermediate having the structure:

wherein R^{x1} and R^{x2} are independently hydrogen, aliphatic, alicyclic or aryl; g is 1, 2, 3 or 4;

L is CR_{L1}R_{L2}, S, O or NR_{L3}, wherein each occurrence of R_{L1}, R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R_{GI} , R_{M1} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent R_{L1}, R_{L2}, R_{L3}, R_{G1}, R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety;

 R_2 is hydrogen, -(C=O) R_C or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein each occurrence of R_C is independently hydrogen, OH, OR_D , or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein R_D is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

 R_6 is hydrogen, -(C=O) R_E or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, wherein each occurrence of R_E is independently hydrogen, OH, OR_F, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein R_F is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety.

63. The intermediate of claim 62 having the structure:

- 64. The intermediate of claim 62 or 63 wherein R^{x1} and R^{x2} are independently hydrogen, alkyl or aryl.
- 65. The intermediate of claim 62 or 63 wherein R^{x1} and R^{x2} are each hydrogen.
- 66. The intermediate of any one of claims 46, 53, 62 and 63 wherein R_2 is hydrogen, or a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl, heteroalkyl, -alkyl(aryl) or acyl moiety.

- 67. The intermediate of claim 66 wherein R₂ is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl, -CH(CH₃)Et, -CH(CH₃)CH₂CH₂CH₃, -CH(CH₃)CH₂CH₂CH₃, -CH₂CH(CH₃)₂, -CH(CH₃)CH(CH₃)₂, -C(CH₃)₂Et, -CH(CH₃)cyclobutyl, -CH(Et)₂, -C(CH₃)₂C≡CH, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl.
- 68. The intermediate of claim 66 wherein R_2 is methyl, ethyl, propyl or *i*-propyl.
- 69. The intermediate of any one of claims 46, 53, 62 and 63 wherein R_6 is methyl, ethyl, propyl, butyl, pentyl, tert-butyl, i-propyl, $-CH(CH_3)CH_2CH_3$, $-CH_2CH(CH_3)_2$, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl; and R_2 is methyl, ethyl, propyl, butyl, pentyl, tert-butyl, i-propyl, $-CH(CH_3)Et$, $-CH(CH_3)CH_2CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH_3$, $-CH_3$, -
- 70. The intermediate of claim 69 wherein R_6 is tert-butyl.
- 71. The intermediate of any one of claims 46, 53, 62 and 63 wherein R_{G1} is hydrogen, substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl or substituted or unsubstituted phenyl.
- 72. The intermediate of claim 71 wherein R_{G1} is hydrogen, methyl or phenyl.
- 73. The intermediate of claim 71 wherein R_{G1} is hydrogen.
- 74. The intermediate of any one of claims 46, 53, 62 and 63 wherein R_{M1} and R_{M2} are each independently hydrogen, hydroxyl, a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl moiety; a substituted or unsubstituted phenyl moiety, or R_{M2} is absent when R_{M1} and the

substitutents on L, taken together, form a substituted or unsubstituted aryl or heteroaryl moiety.

- 75. The intermediate of claim 74 wherein R_{M1} and R_{M2} are each hydrogen.
- 76. The intermediate of any one of claims 46, 53, 62 and 63 wherein L is $CR_{L1}R_{L2}$ wherein R_{L1} and R_{L2} are each independently hydrogen, substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl or substituted or unsubstituted phenyl.
- 77. The intermediate of claim 76 wherein L is CH₂.
- 78. A method for preparing a compound of formula VI^A:

 (VI^A)

said method comprising steps of:

(a) reacting two compounds having the structures:

$$R_6$$
 M_0 R_{G1} OH R_{M1} OH R_{M2}

under suitable conditions to form a compound having the structure:

(b) oxidizing the compound formed in step (a) under suitable conditions to form a compound having the structure:

(c) subjecting the compound formed in step (b) to suitable olefin-forming conditions to form a compound having the structure:

(d) subjecting the compound formed in step (c) to suitable diversification reactions to generate the desired compound having the structure:

wherein g is 1 or 2;

RQ is hydrogen, lower alkyl or an oxygen protecting group;

 R_2 and R_6 are independently substituted or unsubstituted linear or branched lower alkyl;

 R_{10a} is hydrogen or substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

L is CR_{L1}R_{L2}, S, O or NR_{L3}, wherein each occurrence of R_{L1}, R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R_{G1} , R_{M1} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and wherein any two adjacent R_{L1} , R_{L2} , R_{L3} , R_{G1} , R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

- 79. The method of claim 78 wherein, in the step of oxidizing, the conditions comprise Swern or Dess Martin oxidizing conditions.
- 80. The method of claim 78 wherein, in step (c), the olefin-forming conditions comprise $Ph_3P=C(R_{10a})CO_2R^{Q'}$; wherein $R^{Q'}$ is hydrogen, lower alkyl or an oxygen protecting group; and R_{10a} is as defined generally above and in classes and subclasses herein.
- 81. A method for preparing a compound of formula VI^A:

said method comprising steps of:

(a) reacting two compounds having the structures:

$$R_{2}$$
 R_{6} R_{6

under suitable conditions to form a compound having the structure:

wherein R^{X1} and R^{X2} are independently hydrogen, alkyl, heteroalkyl, aryl or heteroaryl;

(b) converting the compound formed in step (a) under suitable conditions to form a compound having the structure:

(c) subjecting the compound formed in step (b) to suitable diversification reactions to generate the desired compound having the structure:

wherein g is 1 or 2;

RQ is hydrogen, lower alkyl or an oxygen protecting group;

 R_2 and R_6 are independently substituted or unsubstituted linear or branched lower alkyl;

 R_{10a} is hydrogen or substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

L is $CR_{L1}R_{L2}$, S, O or NR_{L3} , wherein each occurrence of R_{L1} , R_{L2} and R_{L3} is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R_{GI} , R_{M1} and R_{M2} is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent R_{L1} , R_{L2} , R_{L3} , R_{G1} , R_{M1} or R_{M2} groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

- 79. The method of claim 81 wherein the step of converting comprises steps of:
 - (i) subjecting the compound having the structure:

to ozonolysis conditions to form an aldehyde having the structure:

(ii) subjecting the compound formed in step (i) to suitable olefin-forming conditions to form a compound having the structure:

- 80. The method of claim 81 wherein, in step (ii), the olefin-forming conditions comprise $Ph_3P=C(R_{10a})CO_2R^{Q'}$; wherein $R^{Q'}$ is hydrogen, lower alkyl or an oxygen protecting group; and R_{10a} is as defined generally above and in classes and subclasses herein.
- 81. The method of claim 81 wherein, the step of converting comprises a step of: subjecting the compound having the structure:

to cross-olefin-metathesis conditions in the presence of $CH_2=C(R_{10a})CO_2R^{Q'}$ to form a compound having the structure: